

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace any/all prior versions, and listings, of claims in the application, wherein additions are shown in underlined text and deletions are shown in strike-out text or between double brackets ([[]]):

1.-83. (Canceled)

84. (Currently Amended) A method of producing a comminuted sterile suspension of particles, which comprises:

subjecting an initial sterile suspension of particles to a comminution procedure carried out in a sterilized particle size reduction apparatus, said particle size reduction apparatus comprising an interaction chamber for reducing the particle size of the suspension, ~~[[and]]~~ an intensifier for introducing the suspension into the interaction chamber at high pressure, and a conduit between the interaction chamber and the intensifier, said conduit comprising a sterilizable diaphragm needle valve;
and

recovering a suspension of particles of reduced size;

wherein ~~components of the particle size reduction apparatus are sterilizable~~ and the method comprises sterilization wherein at least surfaces of the apparatus contacting the suspension are sterilized.

85. (Previously Presented) A method according to Claim 84, wherein the sterile suspension comprises Budesonide or Fluticasone.

86. (Currently Amended) A method according to Claim 84, ~~wherein~~ comprising monitoring particle size ~~is monitored~~ until a final particle size in the suspension of mass median diameter ~~2-3~~ 2 μ m - 3 μ m is obtained.

87. (Previously presented) A method according to Claim 84, further comprising packaging the sterile suspension into sterile ampoules.

Claims 88. - 141. (Canceled)

142. (New) The method of claim 84, wherein the intensifier comprises a reciprocating plunger and a bushing assembly to guide the plunger, said bushing assembly comprising a channel in or on the surface of the bushing assembly and wherein said sterilization comprises passing steam or water through the bushing assembly while the plunger is in place.

142. (New) The method of claim 84, wherein the intensifier comprises a plunger rod connected via a threaded cam nut to a connecting rod, at one end of which connecting rod is a screw thread to receive the cam nut, and wherein the dimensions of the screw thread and the thread of the cam nut are such that as the nut is screwed onto the connecting rod respective mating surfaces of the cam nut and the connecting rod mate simultaneously.

143. (New) The method of claim 84, wherein the sterilizable diaphragm needle valve has a metal-to-metal seat.

145. (New) The method of claim 84, wherein the intensifier comprises an output and an input, and the interaction chamber comprises an input and an output, the output of the intensifier being connected to the input of the interaction chamber and the output of the interaction chamber being connected to the input of the intensifier, and wherein there is no conduit between the output of the intensifier and the input of the intensifier other than via the interaction chamber.

146. (New) The method of claim 84, wherein the seal is an annular high-pressure seal for a plunger reciprocating within a barrel, comprising upper and lower body portions being in the form of a cup and having sides surrounding a recess, the sides being outwardly deformable so that respective outer and inner edges of the sides of the cup make, in use, sealing contact with respectively the barrel and the plunger, the seal further comprising a brace to prevent the sides from collapsing into the recess under low pressure and wherein the brace comprises a resilient plastic material.

147. (New) The method of claim 146, wherein said brace presents a smooth surface free from cavities.

148. (New) The method of claim 146, wherein said seal comprises virgin PTFE or glass-strengthened PTFE.

149. (New) A method of producing a comminuted sterile suspension of particles, comprising

subjecting an initial sterile suspension of particles to a comminution procedure carried out in a sterilized particle size reduction apparatus, said particle size reduction apparatus comprising

(i) an interaction chamber for reducing the particle size of the suspension,

(ii) an intensifier for introducing the suspension into the interaction chamber at high pressure,

(iii) a sterilizable diaphragm needle valve in a conduit between the intensifier and the interaction chamber,

(iv) a reciprocating plunger, and

(v) a bushing assembly to guide the plunger comprising a channel in or on the surface of the bushing assembly to allow steam or water to pass through the bushing assembly while the plunger is in place;

sterilizing the particle size reduction apparatus by passing steam or water through the sterilizable diaphragm needle valve and passing steam or water through the bushing assembly while the plunger is in place; and
recovering a suspension of particles of reduced size.